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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,751	08/17/2006	Francese Giancarlo	705152-2001	9535

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EXAMINER	
RAO, SAVITHA M	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,751	GIANCARLO ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 28-46 are pending.

Claims 28-46 are under consideration in the instant office action.

Election/Restrictions

Applicant's election with traverse of Group V (claims 13, 18-24 and 25-27) in the reply filed on 12/01/2008 is acknowledged. The traversal is on the ground(s) that the subject matter of each group of claims is so closely relate to the others, that the search associated with each group overlap with the searches for the others and as such no undue burden exists to examine the claims in a single application.

Examiner finds the applicant's argument unpersuasive and maintains the restriction since as the Groups are patentably distinct and independent since they lack unity as set forth in the restriction requirement dated 10/30/2008 (pages 1-4). The subject matter clearly lacks unity of invention for the reasons given in the restriction requirement and, thus, the claims are directed to patentably distinct inventions and, because of the distinct nature of the inventions, do not constitute overlapping subject matter that would result in a coextensive search.

It is also noted that the Applicant's cancellation of claims directed to the other inventions renders the remarks directed to overlapping subject matter and no undue burden moot as there are no longer any claims pending directed to other inventions.

Restriction for examination purposes as indicated is proper. Thereby the restriction requirement is still deemed proper and is therefore made FINAL.

Amended claims filed on 01/06/2009 are acknowledged, where claims 1-27 were cancelled.

Claims under consideration in the current office action are claims 28-46 which were newly added in the amendment dated 01/06/2009 and read on the elected subject matter of group V.

Applicant timely traversed the restriction (election) requirement in the reply filed on 12/01/2008.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 44-46 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 44-46 provides for the use of the solution which contains either (6S)-sodium folinate or (6S) potassium folinate for the preparation of a medicament., but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

For the purposes of the instant office action claims 44-46 are being interpreted as being drawn to a concentrated stable solution comprising beside water either (6S)-sodium folinate or (6S) potasium folinate .

Claim 28, 39, 40, 41,42 and 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then

narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

Instant Claim 28 recites the broad recitation of the "concentrated stable solution" but further states and "injection or infusion solution" which is a more limited embodiment of the claim, However, the use of the term "especially" does not specifically limit the claim only to those injection or infusion solutions and, thus, it is not clear what is meant to be limiting in the claims (i.e., either the broader embodiment of a concentrated stable solution or the more limited embodiment of, specifically, an injection or infusion solution. Dependent claims 39, 40-42 and 44-46 are accordingly also rendered unclear with respect to this limitation in instant claim 28.

Instant Claim 42 recites the broad recitation of the "an inert gas atmosphere" but further states and "nitrogen atmosphere" which is a more limited embodiment of the claim, However, the use of the term "especially" does not specifically limit the claim only to nitrogen atmosphere, thus, it is not clear what is meant to be limiting in the claims (i.e., either the broader embodiment of a inert gas atmosphere or the more limited embodiment of, specifically, a nitrogen atmosphere

Instant claim 39 recites the broad recitation of the weight of (6S)-sodium folinate or (6S)-potassium-folinate of 2-15% by weight, and the claim also recites, 2-6% by

weight which is a narrower statement and 5% by weight which is a very specific amount. thus, it is not clear what is meant to be limiting in the claims (i.e., either the broadest range of 2-15% or the narrower range of 2-6% or the specific amount of 5% by weight of the folinate)

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 is vague and indefinite in that the metes and bounds of the "the preparation of a medicament for rescues-rescue agent- after the treatment with high doses of methotrexate" are unclear. The term "rescues-rescue agent-" is unclear because there is no clear definition as to what such an agent is, is it an agent which is part of the solution, or is it an agent used in combination with the instantly claimed solution or is it an agent used with the treatment of methotrexate. It would be remedial to clarify the metes and bounds of the term "rescues-rescue agent" in claim 44.

Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28-46 are rejected under 35 U.S.C. 102 (b) as being anticipated by Buchs et. al (US 5814635).

It is respectfully pointed out that claims 29-38 are product-by-process claims. As per MPEP section 2113 (R-1) product by process claims. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113. Thus, because Buchs teaches a product that is identical to what is instantly claimed, then the process limitations, while considered, are not patentably *limiting* to the claims because the prior art teaches an identical product and, therefore, the manner in which it was made fails to apparently result in a product different from that which is already known in the prior art.

Buchs teaches a concentrated stable solution, especially an injection solution characterized in that it contains besides water either sodium-leucovorin or potassium-leucovorin or sodium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid or potassium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid (col.2, lines 15-19). Buchs teaches that N(5)-Formyl-5,6,7,8-tetrahydrofolic acid, also named folinic acid, is used in the form of its calcium salt (calcium-leucovorin USP) as an agent in the cancer chemotherapy (col.1, lines 9-11). Buchs teaches the method of preparation of the concentrated stable solution especially an injection solution where in Folinic acid or N(5)-methyl-5,6,7,8-tetrahydrofolic acid is suspended in degassed water at room temperature under an inert gas atmosphere. The water is acceptable for the preparation of injection solutions. An aqueous solution of

sodium- or potassium-hydroxide, -hydrogen carbonate or -carbonate is added in portions for a sufficient time until a clear solution is formed, which has the desired pH-value. The obtained solution is subjected to sterile filtration, and vials are filled with the resulting sterile solution under an inert gas atmosphere (col. 2, lines 20-32, patented claim 11).

Buchs teaches that the preferred embodiments of his invention comprised more preferably from 2-6% weight of sodium-leucovorin or potassium-leucovorin or sodium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid or potassium-N(5)-methyl-5,6,7,8-tetrahydrofolic acid (col.2, lines 33-39, patented claims 4- 5 and 13-15). Buchs also teaches that the pH-value of the solution is more preferably 8.0 (col.2, line 40-41, patented claims 6-8 and 16) Buchs additionally teaches that his invention also provides a concentrated, stable solution of the bases of folates, which contains neither a stabilizer nor complexing agents (col.2, lines 9-11). Note: It is a position of the examiner that the use of term "completing" in col.2, line 11 is a typo and is actually referring to the "complexing" agent, since the reference discloses that EDTA and similar complexing agents are not acceptable in an injection solution and it is the object of the invention to overcome that drawback in the prior art. Additionally the example of the preparation of the inventive solution does not include any stabilizing and complexing agent (page 2, line 65 to page 3, line 17).

Buchs additionally teaches in example the preparation of inventive solution which comprises the following steps, 200.7 g of folinic acid with a water content of 10.2% by weight were suspended under stirring at room temperature in 2.5 liters of degassed,

sterile water under a nitrogen atmosphere. Then was added drop by drop under stirring a 10% aqueous sodium hydroxide solution until a clear solution has been formed, which had a pH-value of 8.0. The obtained clear solution was diluted to a volume of 3.6 liters by the addition of degassed, sterile water. This diluted solution was subjected to a sterile filtration (pore size: 0.2 micrometer). The obtained sterile filtrate was filled under a nitrogen atmosphere in vials. The vials were stored in a refrigerator at a temperature of 4.degree. C (page 2, line 65 to page 3, line 17).

Buchs also teaches that the solution of his invention can be used in the preparation of a medicament for rescues/rescue agents after treatments with high doses of methotrexate or combined with 5-fluorouracil or used in the preparation of a medicament for the treatment of megaloblastic anemia and dihydropteridin reductase deficiency (col. 2, lines 56-62 and patented claims 17-20).

Accordingly claims 28-46 are anticipated by Buchs et al.

Conclusion

Claims 28-46 are rejected. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7 am to 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAVITHA RAO/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614